REMARKS

With entry of this amendment, claims 32, 34, 36, 37, 39, and 42-44 are under consideration. Applicants amended the specification to further describe the subparts of Figures 6, 7, 11, and 12 and to identify the sequences set forth in Figures 5 and 7. In the amendments, Applicants have identified the exact page number, paragraph number, and line numbers pertaining to each amendment. These amendments do not introduce new matter, as they make express what was implicit in these figures.

To facilitate prosecution and without prejudice or disclaimer, Applicants have amended claims 32, 34, 36, 37, and 39 to recite a pharmaceutical composition comprising at least one of a monoclonal chimeric or humanized antibody to lipoteichoic acid of Gram positive bacteria and a fragment, region, or derivative of the monoclonal chimeric or humanized antibody. This amendment merely incorporates the elements of claims 33, 35, 38, and 40 and is also supported by the specification at page 21, lines 13-15 and page 22, lines 1-4. Thus, no new matter has been introduced. Applicants have canceled claims 33, 35, 38, and 40.

Applicants acknowledge with appreciation the Office's withdrawal of the following rejections: claims 32 and 37 under 35 U.S.C. §112, second paragraph; claims 32 and 33 under 35 U.S.C. §102(e) in view of Gristina et al.; and claims 32 and 33 under 35 U.S.C. §102(b) in view of Fattom et al. (WO93/09811). The Office has also considered Information Disclosure Statement filed on July 14, 2003.

Other rejections of claims 32-40 and 42-44 under the doctrine of obvious-type double patenting and under 35 U.S.C. §§ 112 and 102 are maintained. Applicants

address each of these remaining rejections below according to their judicial and statutory origins.

Sequence Listing and Brief Description of the Drawings

The Office continues to allege that the current Sequence Listing does not comply with 37 C.F.R. §§ 1.821-1.825 because only some of the nucleotide and amino acid sequences set forth in Figures 5, 7A, and 7B are identified with a sequence identification number (SEQ ID NO). As explained, Applicants provide SEQ ID NOS. only for sequences not previously given a SEQ ID NO. Thus, the sequences not assigned a SEQ ID NO are identical to prior sequences in the figure that were assigned a number. To make the resulting SEQ ID NO. designations clear, Applicants have amended the description of these figures to indicate which identical nucleotide sequences and amino acid sequences share the same SEQ ID NO. As the Office's objection to the current Sequence Listing has been obviated, Applicants respectfully request its withdrawal.

The Office also continues to object to the Brief Description of the Drawings because Applicants' prior amendment of the description for Figures 6, 7, 11, and 12 did not precisely state the specific line numbers at which the recited amendments should be made. To facilitate prosecution, Applicants have described these specification amendments according to page number, paragraph number, and line number. As these amendments and their locations in the specification are clear, Applicants request that the Office withdraw this objection.

Rejection Under Obvious-Type Double Patenting

The Office rejects claim 32 for alleged obvious-type double patenting in light of claims 1-6 of U.S. Patent No. 5,955,074 ('074 patent). According to the Office, the method of claim 1 in the '074 patent entails administering directed human immune globulin (DHIG). The process for producing DHIG, the Office believes, includes immunization of a host with TCA extracted antigen, which is comprised of LTA. The Office concludes that immunization of a host with a composition that comprises LTA would generate a pharmaceutical composition that comprises anti-LTA antibodies. Applicants respectfully traverse.

Solely to facilitate prosecution, Applicants have amended claim 32 to recite a monoclonal chimeric or humanized antibody to LTA (or a fragment, region, or derivative of the antibody). A method of treating or preventing an infection caused by Gram positive bacteria using monoclonal chimeric or humanized antibodies is not obvious in view of a method of treating *S. epidermidis* infection using Directed Human Immune Globulin (DHIG). Specifically, issued claim 1 provides a method of preventing and treating *Staphylococcus epidermidis* infections in neonates, comprising administering to said neonates a Directed Human Immune Globulin obtained by the steps: a) obtaining a source of immune globulin from the group consisting of serum, plasma, and an immunoglobulin pool; b) in a binding screen, screening the immune globulin source for specific binding for *Staphylococcus epidermidis* and selecting the source which evidences specific binding; and c) in an activity screen, screening the immune globulin source of step b) for 80% opsonophagocytic bactericidal activity against *Staphylococcus*

epidermidis and selecting a source having at least 80% opsonophagocytic bactericidal activity against *Staphylococcus epidermidis.*

In contrast, the method of pending claim 32 recites a pharmaceutical composition comprising at least one of a monoclonal chimeric or humanized antibody to lipoteichoic acid of Gram positive bacteria and a fragment, region, or derivative of the monoclonal chimeric or humanized antibody. Issued claim 1 of the '074 patent does not suggest or render obvious the use of chimeric or humanized antibodies to LTA. Applicants respectfully request that the Office withdraw this rejection of claim 32 under the judicial doctrine of obvious-type double patenting.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 32-40 and 42-44 remain rejected as allegedly not enabled for the use of any monoclonal antibody (MAb), fragment, region, or derivative that binds SEQ ID NO 1 or 2 or is a derivative of SEQ ID NO 88 or 89 for treating or preventing a Gram positive bacterial infection. Applicants address this rejection as it relates to claims that are under consideration with entry of this amendment. To clarify the record, Applicants note that claim 34 does not only recite MAb 96-110 itself, but also includes the characteristics set forth in independent claim 32, on which claim 34 depends. A similar relationship exists between independent claim 37 and claim 39. Regarding claim 44, this claim recites Complementary Determining Regions derived from MAb 96-110 as compared to other regions, fragments, or derivatives of an antibody.

In the current Office Action (Paper No. 18), the Office believes that the specification does not enable the use of fragments, such as the Fc fragment of MAb 96-110, in treating or preventing a Gram positive infection. The Fc fragment does not

participate in epitope binding and therefore need not be enabled by the specification. But for regions, fragments, and derivatives of an antibody that do bind to LTA, the specification does enable these antibody forms for treating or preventing Gram positive bacterial infections as demonstrated, for example, in Examples 12 and 13.

These examples describe *in vivo* protection experiments in which MAb 96-110 or its chimeric counterpart were used in adult mice or suckling rats. As the specification discusses at page 25, lines 12-18, there are several ways in which antibodies or their fragments, regions, and derivatives can work to protect a host from a Gram positive bacterial infection. Among them are binding to LTA on the bacteria to block initial binding to epithelial cells and binding to LTA to modulate inflammatory responses. These two functions are shared by any antibody region, fragment, or derivative that binds to LTA. In addition, there may also be antibody regions, fragments, or derivatives that, in addition to LTA binding, retain the opsonophagocytic bactericidal activity of the parent antibody. Examples 12 and 13 clearly show the efficacy of an anti-LTA antibody in treating or preventing a Gram positive bacterial infection. Moreover, these examples also provide the skilled artisan with animal models in which other anti-LTA antibodies or fragments, regions, or derivatives thereof can be tested for protection or treatment efficacy.

The Office continues to contend that the effect antibodies have on treating infections can be unpredictable, citing 5 references that allegedly demonstrate this unpredictability. Fiedel and Jackson (*Abstracts of the Ann. Mtg. of the Amer. Soc. for Microbiol.*, p. 104, abstract M146 (1972); "Fiedel") allegedly show that anti-teichoic acid antibodies induced kidney disease in rabbits. Aasjord et al. (*Acta Path. Microbiol.*

Immunol. Scand., 93:245-50 (1985); "Aasjord") allegedly discloses two anti-LTA antibodies that demonstrated equivalent binding specificities as antibodies associated with multiple sclerosis (MS). Stashenko et al. (*Archs. Oral Biol.*, 31:455-61 (1986); "Stashenko") allegedly discloses 5 MAbs against *S. mutans* LTA that enhanced adherence of that bacterium along with *S. salivarius*, *S. sanguis*, and *L. casei.* Wergeland et al. (*J. Clin. Microbiol.*, 27:1286-91 (1989); "Wergeland") allegedly discuss patients with staphylococcal infections that have antibodies to LTA, teichoic acid, and peptidoglycan and still have disease. Yokoyama et al.[1] (*Jibi Inkika Men'eki Arerugi*, 13:50-51 (1994); "Yokoyama") allegedly reports that children with anti-LTA antibodies still have recurrent tonsillitis. The alleged teachings of these references are irrelevant to whether the claimed invention is enabled.

The Office relies on these references to support two premises: (1) that the use of anti-LTA antibodies allegedly may incur negative side effects in a clinical setting; and (2) that the use of anti-LTA antibodies allegedly may not be effective for treating disease in the clinical setting. To support the first premise, the Office looks to Fiedel, Aasjord, and Stashenko, while relying on Wergeland and Yokoyama to support the second premise.

Both of these issues are squarely within the responsibility of the Food and Drug Administration, and not the USPTO. Indeed, these are the issues specifically analyzed by clinical trials per the FDA's guidelines for developing a product for entry into the market. The U.S. Court of Appeals for the Federal Circuit has clearly indicated that

[1] The Office refers to this reference as Yuji et al. The first author of this article is Yuji Yokoyama. To accurately refer to this article, Applicants will use Yokoyama et al. or "Yokoyama."

testing for the full safety and effectiveness of a potential drug is more properly left to the FDA and that such testing is not required by Title 35 in the context of Office proceedings. *See In re Brana*, 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995) (citing *Scott v. Finney*, 34 F.3d 1058, 32 U.S.P.Q.2d 1115 (Fed. Cir. 1994)). By invoking these issues, the Office is confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption." *Id.* at page 1567. The Court further reasoned that

> one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, even though it may eventually appear that the compound is without value in the treatment in humans.

Id. In sum, these issues are not relevant to an enablement assessment by the USPTO.

The specification does enable the invention of claims 32, 34, 36, 37, 39, and 42-44. See Applicants' discussion above regarding Examples 12 and 13. Applicants respectfully request that the Office withdraw its rejection of these claims accordingly.

Rejections Under 35 U.S.C. §102

A reference anticipates a claim when "each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See, e.g., Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The Office continues to reject claim 32 as allegedly anticipated by four references:

1. Claim 32 is allegedly anticipated by Dale et al. (*J. Infect. Dis.*, 169:319-23 (1994); "Dale") under 35 U.S.C. § 102(b) because Dale allegedly teaches the claimed method;
2. Claim 32 is allegedly anticipated by Fischer (WO 93/19373) under 35 U.S.C. § 102(b) because the Office believes that this reference discloses the claimed method and uses a composition comprising antibodies to Gram positive bacteria;
3. Claim 32 is allegedly anticipated by Fattom et al. (U.S. Patent 5,770,208; "Fattom 1") under 35 U.S.C. § 102(e) because this reference allegedly teaches the claimed method and uses antibodies that react with a conserved sugar and two other polysaccharide antigens; and
4. Claim 32 is allegedly anticipated by Ichiman et al. (*Microbiol. Immunol.* 33:277-86 (1989); "Ichiman") under 35 U.S.C. § 102(b) because Ichiman allegedly discloses the claimed method and uses antibodies to unencapsulated Gram positive bacteria.

Solely to facilitate prosecution and without disclaimer or prejudice, Applicants have amended claim 32 to recite a method comprising administering a pharmaceutical composition comprising at least one of a monoclonal chimeric or humanized antibody to LTA of Gram positive bacteria and a fragment, region, or derivative of the monoclonal chimeric or humanized antibody, wherein the monoclonal chimeric or humanized antibody, fragment, region, or derivative thereof binds to LTA at a level of twice background and enhances the opsonization of Gram positive bacteria by 75% or more.

None of the above four references recite or teach, expressly or inherently, chimeric or humanized monoclonal antibodies that bind to LTA and have the opsonic activity set forth in claim 32. Accordingly, none of these references anticipate claim 32. Applicants request that these rejections be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the claims under consideration.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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